UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/688,962	10/21/2003	Gary Levy	9579-80	3922

1059 7590 12/05/2006

BERESKIN AND PARR
40 KING STREET WEST
BOX 401
TORONTO, ON M5H 3Y2
CANADA

EXAMINER	
BOESEN, AGNIESZKA	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/688,962	LEVY, GARY	
	Examiner	Art Unit	
	Agnieszka Boesen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed September 26, 2006 in response to the Office Action of March 28, 2006 is acknowledged and entered. Claims 19-32 have been canceled, claims 33-37 have been added, and claims 33-37 are pending and under examination. New claim 33 finds support in previous claims 19 and 27; new claim 34 finds support in previous claim 28; new claim 35 finds support in claims 29 and 30; new claim 36 finds support in previous claim 20; and new claim 37 finds support in claim 21.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Objections

Objection to claims 19-32 because of reciting non-elected subject matter **is moot** because Applicant canceled claims 19-32.

Objection to claim 31 under 37 CFR 1.75(c), as being of improper dependent form **is moot** because Applicant canceled claim 31.

Objection to claims 24, 27, 28, and 30 because of informalities **is moot** because Applicant canceled claims 24, 27, 28, and 30.

Claim Rejections - 35 USC § 112

Rejection of claim 19, and 20-32 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is moot** because Applicant canceled claims 19, and 20-32.

Rejection of claims 19-32 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention **is moot** because Applicant canceled claims 19-32.

Rejection of claim 22 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and/or use the invention **is moot** because Applicant canceled claim 22.

New claims 33-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and/or use the invention.

The new claims 33-37 are drawn to a method of reducing immune coagulation associated with fgl2 expression, which is the same method as canceled claim 22 was directed to.

Applicant's arguments have been fully considered but were not persuasive. In the enablement rejection in the Office action of March 28, 2006 Examiner stated that, among other factors, there was lack of working examples enabling one skilled in the art to practice the current invention. Applicant argues that existence of working example is only one factor to be considered in determining whether there is undue experimentation and that the absence of

working examples cannot by itself render the invention non-enabled (MPEP 2164.02). Examiners agrees that the absence of working examples cannot by itself render the invention non-enabled, however in the currently maintained rejection, besides the presence of working examples, a number of other factors were discussed, such as the amount of direction or guidance presented, the nature of the invention, the state of the prior art, the relative skill of those in the art, and the predictability or unpredictability of the art.

The state of the prior art indicates that skilled artisan would be unable to reduce immune coagulation in humans using the instant antisense oligonucleotide because the sequences encoding human and mouse fgl-2 genes are dissimilar. Ding et al., (abstract no: 365, reference no: IDS # 4) teaches that the sequence similarity between fgl-2 and hfgl-2 proteins is over 70% and that these proteins are 90% identical in amino acid sequence, but only at the C-terminal end. Therefore, the specific antisense oligonucleotide sequences recited in claims 33-37 would not be complementary to the human sequence of fgl-2 because of 30% difference between the residues mouse and human fgl-2.

Further the skilled artisan would not be able to inhibit immune coagulation associated with fgl-2 expressed by administering an antisense oligonucleotide. Lonnberg *et al.* (Annals of Medicine. 1996; 28:511-522) reviews the state of the art for antisense oligonucleotide and modifications to these compounds that are used to enhance the bioactivity of the oligos. Lonnberg et al., teach that unmodified oligonucleotides are vulnerable to extra- and intracellular nucleases and have a significantly short biological half-life. Although some chemical additions to antisense oligonucleotide increase resistance to enzymes, modified forms of the oligos exhibit decreased binding affinity and specificity to the target sequence. Lonnberg et al., conclude that

while antisense oligonucleotides are attractive chemotherapeutic agents, several significant obstacles, such lack of stability, affinity, specificity and cellular delivery remain to be resolved.

The skilled artisan would doubt that inhibition of LF-A1 binding to fgl-2 would prevent or reduce any fgl-2 associated immune coagulation. Although fgl-2 is directly linked to MHV-3 virus-induced fulminant hepatic failure in mice, fgl-2 is a factor in various diverse disorders, such as cardiovascular disorders, diabetes, gastrointestinal diseases, fetal loss syndrome, and bacterial and viral infections, see Yuwaraj et al., (Genomics. 2001; 71: 330-338). Therefore, administering an antisense oligonucleotide to inhibit binding between LF-A1 and fgl-2 would not prevent or reduce immune coagulation associated with fgl-2 in all of the various disorders. . Yuwaraj et al., teach that the function of human fgl-2 is not clearly defined and the specific factors determining fgl-2 expression in humans are not known. Yuwaraj et al., also teach that is not known whether allelic variants exist in the fgl-2 gene or if the gene represents an inherited molecular determinant in human hepatitis. There is no nexus in the art between human fgl-2 and hepatitis infection.

Even if these concerns were overcome, the skilled artisan would doubt that the instant, undescribed antisense oligonucleotide inhibitors would have the desired effect on the immune coagulation associated with fgl-2 expression in murine hepatitis virus infection. The working examples in the specification teach that the induction of fgl-2 is not always in murine models of hepatitis virus, see pages 24-27, which discuss the inability of MHV-2 to induce transcription of fgl-2. The working examples demonstrate the lack of predictability for fgl-2 expression and its putative role in every type of murine hepatitis. Therefore, the skilled artisan would not conclude that the instant antisense oligonucleotide inhibitor would be effective in hepatitis infection

because of the discrepancies observed in the murine viruses and the different functions of fgl-2 in murine hepatitis.

Thus, in addition to the lack of working examples, the state of the prior art and the unpredictability of the art indicates that the skilled artisan would be unable to reduce immune coagulation by administration of antisense oligonucleotide that is complimentary to a sequence in the promoter region of fgl2. Therefore the rejection is maintained.

Claim Rejections - 35 USC § 103

The rejection of claims 19-23, 25-26, and 29 under 35 U.S.C. 103(a) as being unpatentable over Ding et al. (Journal of Virology. 1997; 71 (12): 9223-9230) and Mizutani et al. (Journal of Veterinary Medical Science. 1994; 56 (2): 211-215, abstract only) **is moot** because Applicant canceled claims 19-23, 25-26, and 29.

The subject matter of new claims 33-37 is not taught or fairly suggested by Ding et al. nor Mezutani et al. because neither Ding nor Mizutani et al. teach that immune coagulation can be reduced by administering an antisense oligonucleotide that is complementary to a sequence comprising nucleotides 957 to 1032 of SEQ ID NO: 1, which is the promoter region of fgl2, and specifically the LF-A1 binding element of the promoter region.

Conclusion

Applicant's amendment necessitated the new ground of rejections presented in this Office action. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen, Ph.D. whose telephone number is 571-272-8035. The examiner can normally be reached on M – F (9:00AM – 5:30PM). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AB
Agnieszka Boesen, Ph.D.

11/30/06

Stacy B. Chen 12/1/06

STACY B. CHEN
PRIMARY EXAMINER